IN THE DRAWINGS:

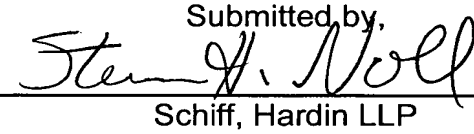
Figures 2 and 6 have amended as shown on the replacement sheets attached hereto.

REMARKS:

The present Amendment makes editorial changes in the specification claims and drawings, and adds an Abstract, to conform the present PCT application to the requirements of United States patent practice. Claims 1-17 have been cancelled solely because the amount of strikethroughs and underlining that would have been necessary to confirm those claims to the requirements of 35 U.S.C. §112, second paragraph would have been unduly burdensome and confusing. No change in the claim language between claims 1-17 and the claims presented herein has been made for the purpose of distinguishing any claims over the teachings of the prior art of record. Accordingly, no change in the claim language is considered by the Applicants as a surrender of any of the subject matter encompassed within the scope of original claims.

Early consideration of the application is therefore respectfully requested.

Submitted by,



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~~**A CONGESTIVE HEART FAILURE MONITOR**~~

~~***Technical field***~~

SPECIFICATION

TITLE

"A CONGESTIVE HEART FAILURE MONITOR"

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to a congestive heart failure monitor.

~~***Background***~~

Description of the Prior Art

Electrical stimulation therapy of congestive heart failure is ~~previously~~ known. Thus in ~~US 5 584 868~~ United States Patent No. 5,584,868 a dual-chamber pacemaker designed for treating congestive heart failure (CHF) by changing the AV interval is described and in ~~US 6 223 079 B1~~ United States Patent No. 6,223,079 a four chamber pacing system for improving cardiac output of CHF patients by controlling pacing to maintain the ventricular mechanical synchronization is disclosed. For providing suitable timing in the latter system impedance sensing in the left heart is used.

Incipient CHF is often present without the patient knowing it. An indicator for incipient CHF would therefore be of great value since treatment by addition of drugs or electrical stimulation therapy could then be introduced at an early stage of CHF to slow down the progression of CHF. This would prolong the survival of the patient. Such an indicator could also be used to alert the patient or the physician about new conditions so appropriate measures can be taken. The first sign of a CHF can be seen in the left atrium, for instance in volume changes thereof.

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SUMMARY OF THE INVENTION

~~The purpose~~ An object of the present invention is to utilize ~~this~~ the above-described knowledge to provide a congestive heart failure monitor for detecting CHF at an early stage.

~~***Disclosure of the invention***~~

~~This purpose is obtained by a congestive heart failure monitor according to claim 1.~~

The first sign of a CHF can be observed in the left atrium of the heart by monitoring its mechanical behavior ~~behaviour~~, like volume changes, as mentioned above. If the pumping ability of the left ventricle is reduced the volume of the left atrium will increase due to the excessive filling of blood. The filing pattern of the left atrium can be disturbed due to mitral regurgitation caused by either diastolic or systolic dysfunction. The diastolic dysfunction could be a result of prolonged PR interval, i.e. the P-wave to QRS interval, or too long an AV interval, resulting in reversed flow back to the left atrium during diastole ~~as~~ because the mitral valve does not close immediately after the atrial contraction. The systolic dysfunction could be a result of infarctic areas in the left ventricle, which disturbs the left ventricle contraction propagation so that the mitral valve cannot close properly, (the papillar muscle ~~get~~ becomes asynchronous), bringing reversed flow back to the left atrium during systole. The systolic dysfunction in the left ventricle could also be a result of bad timing of the right and left ventricle stimulations (e.g. septum, innervated at RVOT stimulation, is involved in the left ventricle contraction) causing mitral regurgitation and disturbed filling pattern of the left atrium. All these conditions ~~results~~ result in a disturbed filling pattern of the left atrium, which ~~and~~ is one of the first signs of CHF.

A first sign of CHF can thus be observed in the left atrium and since the conductivity of blood is different from that of tissue the monitor according to the invention ~~comprises~~ has an impedance measuring unit ~~adapted to measure~~ that measures impedance between at least two electrodes intended to be implanted in

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the patient such that a change in the left atrium volume results in a change in the measured impedance. In this way not only incipient CHF can be detected but also the monitor according to the invention can ~~also~~ be used as a diagnostic tool for studying the progression or regression of CHF for enabling proper treatment of the patient.

~~According to advantageous embodiments~~ In an embodiment of the monitor according to the invention the analyzing ~~means comprise~~ unit includes an averaging ~~means provided to form~~ unit that forms a mean (average) value of the measured impedance during a ~~plurality~~ number of cardiac cycles and the analyzing ~~means are adapted to analyze~~ unit analyzes the mean value to detect CHF. Alternatively, the ~~or said~~ analyzing ~~means comprise~~ unit can include a quotient determining ~~means provided to determine~~ unit that determines the quotient between the impedance minimum and maximum values during a cardiac cycle, and the analyzing ~~means are adapted to analyze~~ unit analyzes the quotient to detect CHF. Preferably the analyzing ~~means are adapted to analyze~~ unit analyzes both the impedance mean value and the quotient to detect CHF. Firstly, even though the impedance changes continuously during the heartbeat, the mean value will decrease when the left atrium volume increases. Secondly, the quotient between the impedance minimum and maximum values will be larger, with increasing blood filling of the left atrium. Accordingly with the present invention an efficient CHF monitor is provided based on the analysis of these two quantities.

~~According to other advantageous embodiments~~ In a further embodiment of the monitor according to the invention the electrodes are designed for implantation in the right and left atria, respectively, or for implantation in the right atrium and left ventricle. In ~~case of~~ an implantable monitor, one of the electrodes can be designed for implantation in the left atrium and the other electrode be formed ~~of~~ by the outer capsule of the monitor, e.g. the pacemaker capsule when the monitor is included in a pacemaker.

Also other combinations of the above mentioned electrodes can be used for the impedance determination.

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The electrodes intended for implantation in the left atrium and the left ventricle are preferably designed for implantation in a coronary vein. For all these alternatives signals corresponding to the blood filling of the left atrium are obtained from the electrodes.

~~According to still other advantageous embodiments~~ In another embodiment of the monitor according to the invention the impedance measuring unit ~~comprises~~ includes a measuring circuit in the form of synchronous demodulator for obtaining both the real and imaginary parts of the impedance, and the impedance measuring unit ~~is~~ preferably ~~adapted to determine~~ determines the impedance phase ~~angel~~ angle for detecting and the ~~analysing means is adapted to analyse~~ analyzing unit analyzes the phase angle for detecting an incipient CHF. Since blood is resistive, a high degree of blood filling results in a small phase angle. On the contrary, if more heart tissue is present, ~~like~~ as in ~~case of~~ a healthy heart, the phase angle will ~~get~~ exhibit a larger negative value.

~~***Brief description of the drawings***~~

~~To explain the invention in greater detail embodiments of the monitor according to the invention chosen as examples will be described below with reference to the enclosed drawings, on which figure 1 illustrates principally the impedance measurements performed in one embodiment of the monitor according to the invention, figure 2 is a simplified illustration of an embodiment of the monitor according to the invention, figure 3-5 illustrate alternative ways of performing impedance unit of the monitor according to the invention, and figure 7 is a flow chart illustrating the signal processing in an embodiment of the monitor according to the invention.~~

~~***Detailed description of embodiments***~~

DESCRIPTION OF THE DRAWINGS

Figure 1 schematically illustrates an impedance measurement performed in an embodiment of the monitor according to the invention.

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Figure 2 is a schematic illustration of the basic components of the monitor according to the invention.

Figures 3-5 respectively illustrate alternatives for performing impedance measurements in the monitor according to the invention.

Figure 7 is a flow chart showing the basic steps in one embodiment of the operation of the monitor according to the invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Figure 1 illustrates ~~principally~~ measurement of the impedance Z between the right atrial lead 2 and the coronary sinus lead 4. As the left atrium is dilated due to CHF the impedance Z will decrease. Also the variation of the impedance between maximum and minimum values will then decrease due to increased wall tension.

To secure a safe fixation of the left atrial electrode 6 in the coronary sinus CS or the great cardiac vein it is beneficial to use a screw-in electrode, cf. figure 2. The optimal right atrial RA electrode 2 position is lightly to be in the inter-atrial septum near the coronary sinus ostium, see the electrode tip 10 in figure 3. With the electrodes 6, 8; 10, 11 positioned as shown in figures 2 and 3 the volume of the left atrium is positioned between the electrodes. This enables variations of impedance variations across the left atrium and a high sensitivity to left atrium volume changes.

Also, other bipolar electrode measurements set-ups as well as tripolar electrode settings are possible in the monitor according to the invention.

The embodiment of the monitor according to the invention shown in ~~figure~~ Figure 2 ~~comprises~~ includes monitor electronics 7 for analysis of the measured impedance for detection of an incipient CHF. An implantation monitor is preferably also provided with telemetry means, not shown in ~~figure~~ Figure 2, for communication with an external programmer and data acquisition device 9.

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Figures 3-5 illustrate quadropolar electrode configurations suitable for use in the monitor according to the invention. In ~~figure~~ Figure 3 the coronary sinus CS lead 12 is positioned on the left atrium and in the ~~figures~~ Figures 4 and 5 the CS lead 14 and 16 respectively is placed on the left ventricle.

The method of bio-impedance measurement is not critical in the monitor according to the invention. Figures 3-5 illustrate a technique wherein an electric current i(t) is supplied between two electrodes and the resulting evoked voltage response v(t) is detected. In the embodiments shown in figures 3 and 5 the evoked voltage response i(t) is supplied. Figure 4 shows an embodiment in which the current i(t) is supplied between a right atrial electrode 17 and a stimulator can 19, whereas the evoked voltage response is measured between the right atrial electrode 17 and a left ventricular electrode 18 positioned in the coronary sinus.

Figure 6 shows an alternative embodiment of the impedance-measuring unit of the monitor according to the invention in the form of a synchronous demodulator. Generally the electric current i(t) is applied to two electrodes 20, 22 and the resulting evoked response is measured between two measurement electrodes 24 and 26. The measured voltage signal is amplified in an amplifier 28. The measured voltage signal is synchronized with the current i(t) with the aid of a reference signal picked up from the current source 21 and supplied to a synchronizing ~~means~~ unit in the form of multiplier 30. A low-pass filter 32 is provided to filter the output signal from the multiplier 30. The resulting impedance Z_1 is the given by the expression

$$Z_1 = u_1 / i$$

where u_1 denotes the filtered resulting synchronized output voltage signal.

With the impedance measuring circuit shown in ~~figure~~ Figure 6 both the real and the imaginary parts of the impedance are measured and consequently the impedance phase angle is obtained as well ~~too~~.

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As discussed above, at left ventricular dysfunction the left atrium will dilate according to the progress of the disease, because the left ventricle is not able to eject blood into the body and blood will consequently stagnate in the left atrium and pulmonary veins. Left atrium blood pressure will increase as well as left atrium wall tension. The blood volume in the left atrium will also increase while the variation between maximum and minimum volume values will decrease. These phenomena can be determined from the measured impedance.

Figure 7 is a flow chart illustrating an example of an embodiment of the monitor according to the invention analyzing ~~analysing~~ the impedance minimum-maximum quotient and the overall impedance mean value for detecting an early CHF. The impedance raw signal obtained as explained above is pre-filtered, at 34 in ~~the figure~~ Figure 7. The filtering at 34 is performed to remove ~~artefacts~~ artifacts of noise, breathings etc. ~~Mean~~ The mean (average) value of the impedance signal during the last heart cycle is calculated in averaging ~~means~~, at 36, and long time mean value calculation is performed by ~~means of~~ a low pass filter, at 38. The expression "long time" could mean a time of the order of typically 10 minutes in this connection.

At 40 in ~~figure~~ Figure 7 the quotient between the impedance minimum and maximum values is determined. The obtained long term mean value and the quotient between minimum and maximum values are compared with predetermined reference or normal threshold values in comparison means, at 42 in ~~the figure~~ Figure 7. The results of these comparisons are used, at 44, to classify the patient's condition according to predetermined built-in rules.

The processing described above with reference to ~~figure~~ Figure 7 can advantageously be used together with an activity sensor and a posture sensor. The impedance properties can then be calculated during the same conditions for the patient, for instance with the patient in a resting supine position. The processing chain of ~~figure~~ Figure 7 can also preferably contain a memory for saving the time history of calculated parameters for further evaluation in external devices, cf. ~~figure~~ Figure 2.

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Although modifications and changes may be suggested by those skilled in the art, it is the invention of the inventors to embody within the patent warranted heron all changes and modifications as reasonably and properly come within the scope of their contribution to the art.